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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/771,418 | 02/05/2004 | Henrik S. Olsen | PF363C2 | 4060 |

22195 7590 04/21/2005

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| EXAMINER | |
|---|---|
| BELYAVSKYI, MICHAIL A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/771,418 | OLSEN ET AL. | |
| | Examiner | Art Unit | |
| | Michail A. Belyavskyi | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *23-82* is/are pending in the application.

4a) Of the above claim(s) *37-39, 54- 56, 67-69, 80-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-36,40-53,57-66 and 70-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 02/15/05 is acknowledged.

Claims 23-82 are pending.

2. Claims 37-39, 54- 56, 67-69, 80-82 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

3. Claims 23-36, 40-53, 57-66 and 70-79 reads on an isolated antibody that specifically binds to an FcR-V polypeptide of claims 23 , 40, 57 and 70 are under consideration in the instant application.

4. Applicant's declaration stating that the deposit of FcR-V clone has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809 have been met ( see Applicant's arguments filed on 02/15/05), has obviated the previous rejection of claims 40-53 and 70-79 under 35 U.S.C. 112 first paragraph regarding the deposit issue.

In view of the amendment, filed 02/15/05 the following rejections remain:

5. 35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

6. Claims 23-36 and 40-53, 57-66, 70-79 stand rejected under 35 U.S.C. 101 as the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the same reasons set forth in the previous Office Action, mailed on 10/15/04.

Applicant's arguments, filed 02/15/05 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) based in part on homology to the Fc-γ2 receptor, the FcR-V polypeptides are important in the regulation of the immune and hematopoietic system and are thought to function as an important trigger of complex immune responses including phagocytosis, antibody-dependant cellular cytotoxicity and release of inflammatory mediators; (ii) the specification teaches that the FcR-V polypeptides are useful for the diagnosis or treatment of specific immune system-related disorders, as recited on page 60, paragraph 0135; (iii) post-filing reference Tedla et al., corroborate the specific and substantial utility described in the specification.

Contary to Applicant's assertion as has been discussed in the previous Office Action, the specification disclosed a purified polypeptide of SEQ ID NO: 10 encoding a novel protein FcR-V ( see page 4, paragraph 0012 and page 16, paragraph 0032 in particular). The specification fails to provide sufficient objective evidence of any activity for encoded protein. Applicant only states that said protein shows sequence homology with many FcRs and KIRs , for example about 55.5 % similarity with bovine Fc-γ2 receptor. The Specification further disclosed that FcR-V may be involved in regulation of the immune and hematopoietic systems . ( see overlapping pages 4-5, paragraph 0012 and page 18, paragraph 0037 in particular). Based upon homology to related molecules the specification disclosed that said protein may play a role in one or more aspects of regulating the immune system and tumor cell biology ( page 58 , paragraph 0131 in particular). It is also said that novel FcR-V protein is broadly expressed in various cells and tissues (page 13, paragraph 0024 in particular). The specification also disclosed that antibody that specifically recognized polypeptide of SEQ ID:10 are useful to provide immunological probe for differential identification of the tissue or cell type or for treating various diseases ( see page 14, paragraph 0025 and page 68, paragraph 0162 in particular).

There is no information pertaining to the significance of the percentage homology, e.g. whether there were any conserved motifs that would led the artisan to accept the protein's function. Moreover, neither the specification nor the prior art disclose any information regarding the evolutionary significance of this homology or relative conservation of structure and function across species. For example, there is no evidence of record showing why homology to a bovine Fc-γ2 receptor would provide a better basis for assigning protein function than homology to a primate species. It is noted that homology search analysis shows that polypeptide of SEQ ID NO:10 shows 63 % amino acid sequence homology to human gp49 polypeptide or 63 % homology to LIR polypeptide or 50 % homology to murine regulation protein p91 ( see attached sequence search analysis). Identifying a protein as having a limited homology to said proteins does not indicate what function it might have. No well-established utility for a FcR-V protein encoded by SEQ ID NO:10 is indicated. After further research, specific and substantial utility might be found for claimed polypeptide of SEQ ID NO:10 and antibody, that specifically recognized said polypeptide. This further characterization, however is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. A well-established utility is a specific, substantial, and utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material.

In support, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) disclose that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Attwood *et al.* (Science, 2000, 290, 471-473) teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable. Given the above information, and in light of the art recognized fact that minor sequence differences can significantly affect a protein's function, one skilled in the art would find it more likely than not that SEQ ID NO:10 is not human Fc-γ2. Thus, the homology-based assignment FcR-V as human Fc-γ2 receptor does not appear to provide evidence of a specific and substantial utility based on the knowledge of the skilled artisan and the data presented in the instant specification.

A utility such as chromosome localization would apply to virtually every naturally occurring polynucleotide and is therefore not specific. Likewise, tissue-specific or cell –specific expression does not rely on specific properties or functions of the encoded protein. Each polypeptide encoded by specific amino acid sequence is expressed within a multicellular organism in some cell type and this expression is regulated in either a temporal or spatial manner. That, is, each expressed sequence is expressed in some cell type at some point in a hosts lifetime. Some polypeptide are expressed embryonically, others are expressed only in particular cells, while still others are expressed in a wide variety of cells. In addition, some polypeptide which are expressed in particular cells are only expressed in response to certain metabolic or environmental stimuli. Therefore, mere expression does not appear to provide evidence of a specific and substantial utility based on the knowledge of the skilled artisan and the data presented in the instant specification.

With regards to the issue that "the specification teaches that the FcR-V polypeptides are useful for the diagnosis or treatment of specific immune system-related disorders, as recited on page 60, paragraph 0135". The passage pointed by Applicant only generally stated that FcR-V polypeptides may be useful for diagnosis or treatment of various immune system-related disorders involving abnormally high or low expression of FcR-V activities. In other words, at the time the invention was made Applicant does not know and does not disclose any specific diseases or conditions known to be associated with the FcR-V polypeptide , encoded by SEQ ID NO:10 or any conditions associated with altered levels (increase or decrease) of said polypeptide. Since any protein or antibody to said protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use of FcR-V polypeptide or antibody to said polypeptide as a treatment agent and therefore, this utility would not be considered to be substantial. Therefore, identification of antibody that binds specifically to FcR-V polypeptide

would not be sufficient to identify or confirm a "real world" context of use; clearly further research would be required to identify a disease in which the encoded protein is involved that can be treated using said antibody.

The instant claims are drawn to an antibody that specifically recognized FcR-V polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support the conclusion that FcR-V polypeptide of the instant application or antibody that specifically recognized said polypeptide was, as of the filling date, useful for therapeutic and diagnostic application, as stated on page 58, paragraph 0131 or for treatment , as stated on page 68, paragraph 0162. Until some actual and specific significance can be attributed to the polypeptide identified in the specification as FcR-V polypeptide, one of the ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

Thus, the disclosed utilities do not appear to be either specific or substantial because the specification fails to disclose a specific and substantial utility for a polypeptide of SEQ ID NO:10. Therefore it appear that a polypeptide of SEQ ID NO:10 and antibody that binds specifically to said polypeptide constitute research reagents for further experimentation to discover a "real world " utility for the claimed invention.

With regards to Applicant's statement that "post-filing reference Tedla et al., corroborate the specific and substantial utility described in the specification".

Contrary to Applicant's assertion, Tedla et al ., only teach that human eosinophils and neutrophils have a restricted patter of cell-surface LIR expression with LIR3 and LIR7 being expressed in almost all donors. Tedla et al., further teach that LIR7 may have a possible function in tempering Th2 cell dependent inflammatory response however, the is no recitation of FcR-V polypeptide or possible function of said polypeptide in inflammatory response. Moreover, it is noted that the sequence of LIR-7 polypeptide has been disclosed by Borger et al., not by Tedla et al., and sequence alignment of the claimed SEQ ID NO:10 does not show 100% identity over the referenced polypeptide as asserted by Applicant ( see attached sequence alignment). Moreover, as has been discussed supra, the current state of the art is that making functional assignments merely on the basis of some degree of similarity between sequences is unreliable.

Thus, for the above mentioned reasons there does not appear to be either a specific and substantial asserted utility, or a well-established utility for the claimed : an isolated antibody that binds specifically to an Fc RV-polypeptide of Claims 23 , 40, 57 and 70 .

In addition, since an FCR-V -polypeptide of Claims 23 , 40, 57 and 70 and antibody to said polypeptide appears to constitute a research reagent, an isolated cells and hybridoma that produces said antibody also do not appear to have a specific and substantial utility, or a well established utility.

Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 23-36, 40-53, 57-66 and 70-79 also stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility for the reasons set forth in the rejection under 35 USC101 above, one skilled in the art clearly would not know how to use the claimed invention for the same reasons set forth in the previous Office Action, mailed on 10/15/04.

Applicant's arguments, filed 02/15/05 have been fully considered, but have not been found convincing.

Applicant asserts that in view of the present application disclosure of a specific and substantial asserted utility for FcR-V proteins, one skilled in the art would know how to use the claimed invention.

Contrary to Applicant's assertion, as has been discussed supra, it is the Examiner position that claimed FcR-V protein and antibody that specifically binds to said protein do not have a specific and substantial asserted utility. Thus one skilled in the art clearly would not know how to use the claimed invention.

9. Claims 57-66 and 70-79 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, mailed on 10/15/04. **This is a New Matter rejection**

"An isolated antibody or fragment thereof that specifically binds a FcR-V protein expressed on the surface of a cell" claimed in claims 57-66 and 70-79 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from. The specification and the claims as originally field only support an isolated antibody, that binds specifically to an FcR-V polypeptide recited in Claims 19, 23 and 40.

Applicant's arguments, filed 02/15/05 have been fully considered, but have not been found convincing.

Applicant asserts that page 2, paragraph 0006, pages 8-11 and pages 56-57 of the instant Specification support for claims 57-66 and 70-79.

Contrary to Applicant's assertion, the passages point by the Applicant do not support for "An isolated antibody or fragment thereof that specifically binds a FcR-V protein expressed on the surface of a cell" claimed in claims 57-66 and 70-79. Moreover, it appears that Applicant mistakenly assumes that the disclosure of " cell expressing FcR-V" is an equivalent of "FcR-V protein expressed on the surface of a cell". The genus of "Cells expressing FcR-V" reads on soluble FcR-V and membrane-bound FcR-V, while subgenus "FcR-V protein expressed on the surface of a cell " reads only on a membrane-bound form of FcR-V. See *In re Smith* 173 USPQ 679, where it was ruled that a genus may not support a subgenus even though there is a disclosed species within the subgenus.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April 7, 2005

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